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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,044	04/02/2004	Young Hoon Park	A36218	3943

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EXAMINER

ARCHIE, NINA

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/817,044

Applicant(s)

PARK ET AL.

Examiner

Nina A. Archie

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,8-13,23 and 24 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5,8-13,23 and 24 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☒ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. ____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____.

DETAILED ACTION

The response filed 8-31-06 has been entered into the record.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The drawings were received on 4/02/04. These drawings are acceptable.

Specification

The specification is objected to because of the following informality: reference on p. 4 is not clear as it is stated in the specification Dang et al., *E.coli* and *Salmonella*, 1:191-102, 1996. Appropriate correction is required.

Information Disclosure Statement

Applicants have not filed an information disclosure statement in this application.

Election/Restrictions

Applicant's election of Group I, claims 1-5, 8-13, 23 and 24 in the response filed 8-31-06 acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 6, 7, 14-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed 8- 31-06.

It is noted that Applicants request rejoinder when the claims of Group I become allowable.

Claim Objections

Claim 13 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 13 is drawn to isolated and purified strain of *Escherichia coli* wherein the strain is *Escherichia coli* is FTR2717. The specification teaches that FTR2717 does not comprise an endogenous gene, nor does

comprise exogenous genes as required by claim 9. Therefore, claim 13 as depending from claim 9, is broadening.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, purity of naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui 156 USPQ 426 (1966). However when purity results in new utility, patentability is considered. Merck co. V. Chase Chemical Co. 273 F. Supp 68 (1967). See also American Wood v. Fiber Disintegrating Co., 90 US 566 (1974); American Fruit Growers v. Brogdex Co. 283 US 1 (1931); Funk Brothers Seed Co. V. Kalo Inoculant Co. 33 US 127 (1948). In the instant case recitation of an inactivated gene does not indicate the hand of man because naturally occurring mutations can inactivate genes as such, the claimed *Escherichia coli* strains are deemed products of nature.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make sure the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Art Unit: 1645

Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 8 requires an inactivated chromosomal *pckA* gene(s). Claims 9-12, require the strain to have endogenous and exogenous *ppc* genes. A "gene (cistron)" is defined as a segment of DNA involved in production of a polypeptide chain; it includes regions preceding and following the coding region (leader and trailer) in "Genes IV" Benjamin Lewin 1990. However, the specification teaches deletion of the endogenous *ppc* "gene" but does not teach addition of exogenous *ppc* genes in the chromosome nor how to inactivate such. Therefore, the *E. coli* strains described in the specification necessarily lack an endogenous *ppc* gene and cannot have an exogenous *ppc* gene since the fragments produced by the process of claim 2 are not a "gene" by definition because they do not code for a polypeptide chain that functions as a *ppc* enzyme. Therefore, the specification lacks written description of the claimed strains of *E. coli* since the *E. coli* strains described in the specification lack endogenous and exogenous *ppc* genes. This issue is best resolved by Applicants pointing to the specification by page and line number where description of the claimed strain is set forth.

Claims 5, 13 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims require the particular *E. coli* strain FTR2717 (KCCM-10475). The specification teaches that this strain was derived from a parent strain parent strain of *E. coli* strain TRN212 (accession number: KCCM-10353) that was developed from inventors from Korean Patent Application No. 2002-015380. The parent strain is not publicly available and the sequences used to derive the daughter strain are not particularly described. Therefore, the skilled artisan could not reproducibly make the claimed *E. coli* strain. As such, a deposit for patent purposes is required.

The specification at page 11, paragraph [0031] provides for the deposit at the Korean Culture Center of Microorganisms under the terms of the Budapest treaty. Applicant's referral to the deposit of the *E. coli* strain insufficient assurance that all required deposits have been made and all the conditions of 37 CFR §1.801-1.809 have been met. If the deposit has been made under the provisions of the Budapest

Art Unit: 1645

Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Claims 9-13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 9-13, independent claim 9 recites the phrase "wherein the strain has resistance to threonine analogues, lysine analogues, isoleucine analogues and methionine analogues compared to a corresponding wild-type strain thereof". However, neither the claim nor the specification clearly defines nor sets forth the meaning or means to assess "resistance to". "Resistance to" has no art defined meaning with respect to amino acids or analogs thereof. Therefore, the skilled artisan would not be readily apprised of the metes and bounds of "resistance to" nor how to assess such. It is unclear how to interpret what is considered "resistance to" and inasmuch as it is not a recognized term and not defined in the specification. Further, claim 9, section (b) appears incomplete because the listing of features of the chromosome are incomplete in that there is no "and" or "or" after feature (b)(3) to indicate the finality of the list of chromosomal structural feature(s).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (EP1347057A1; published 9-24-03) patent in view of Sujimoto et al US patent 5919694 issued July 6, 1999.

Claim 1 is drawn to an *Escherichia coli* strain comprising both *tdcBC* and *pckA* genes that are inactivated and Claim 8 is drawn to an isolated and purified *Escherichia coli* strain having an inactivated chromosomal *tdcBC* gene and an inactivated chromosomal *pckA* gene. At the outset it is noted that Applicants' specification acknowledges that the *pckA* gene and *ppc* gene encode the same enzyme but have alternate gene names in the literature (see page 4, paragraph [0008]).

Park et al (EP1347057A1) teaches an *E. coli* strain for the production of threonine. The *E. coli* strain is genetically engineered in that the *tdcBC* operon of a threonine-producing *Escherichia coli* strain is inactivated by cleaving a site in *tdcB* and *tdcC* of the *tdc* operon and inserting a cassette with the DNA fragment $\Delta tdc::loxpan$ into the cleavage site. Park et al teaches that the *tdcB* and *tdcC* gene fragment including DNA fragment $\Delta tdc::loxpan$ discussed above is inserted into the genome of the *Escherichia coli* strain to allow homologous recombination between the DNA gene fragment $\Delta tdc::loxpan$ and *tdc* gene on the chromosome to elute recombinant strains having the deactivated *tdc* gene (see page 4, [0022-0030]). Park et al teaches that *Escherichia coli* strain with the operon interrupted can enhance the expression of the *ppc* gene (also known as *pckA*; see page 4, paragraph [0008] of the instant specification) involved in the conversion of phosphoenolpyruvate to a threonine biosynthesis precursor and the activity of the threonine dehydratase which is an enzyme that encodes for *tdc* gene which is deactivated in the chromosome and therefore suppresses the threonine metabolic pathway by inhibiting the degradation of threonine while the function of the host microorganism remains active to maximize the

Art Unit: 1645

production of L-threonine in *Escherichia coli* strains (page 3, paragraphs [0017-0020]). Park et al differs by incorporating an extra exogenous phosphoenolpyruvate carboxylase (ppc) genes into the chromosome of the *E. coli* strain with the inactivated tdc operon, as opposed to inactivating the ppc gene.

Sujimoto et al US patent 5919694 teaches a strain of *E. coli* that produces L-threonine. The strain of *E. coli* has a mutant ppc gene that provides for inactivation of the feedback inhibition by aspartic acid (column 2, lines 40-55). Sugimoto teaches how the production of L-threonine can be controlled by feedback inhibition when aspartic acid inhibits the activity of the ppc gene in *Escherichia coli*. The inhibition of aspartic acid is desensitized by replacing an amino acid at a specific site of the ppc gene of *Escherichia coli* with another amino acid without losing the enzyme activity of ppc gene. Therefore, the DNA fragments coding for the mutant ppc gene in *Escherichia coli* can be obtained by recombinant DNA by introducing amino acid replacement, insertion, or deletion into a ppc gene as a wild type enzyme. The mutant ppc gene is introduced into a threonine producing *Escherichia coli* strain which can generate an improved threonine producing *Escherichia coli* strain (see US patent 5919694 Table 4).

It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to inactivate the aspartic acid feedback regulation of ppc by mutating the ppc gene of the *E. coli* L-threonine tdc operon inactivated strain of Park et al to produce an *E. coli* strain producing L-threonine because each of Park et al and Sujimoto et al teach that the deletion of tdc operon and inactivation of feed back inhibition of the ppc gene in an L-threonine producing *Escherichia coli* strain provide for increased recovery of L-threonine from the fermentation culture supernatant.

Citation of Relevant Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ozaki et al. Agric. Biol. Chem. 47 No. 7 (1983) 1569-1576 teaches factors that cause an increase in lysine production using various mutants.

Status of the Claims

No claims are allowed.

Art Unit: 1645

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina Archie whose telephone number is 571-272-9938. The examiner can normally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Bruce Campbell can be reached on 571-272-0974.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Nina Archie
Examiner
Art Unit 1645

Patricia A. Duffy
PATRICIA A. DUFFY
PRIMARY EXAMINER